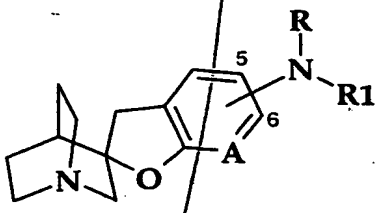
CLAIMS

1. A compound of formula I,



I

wherein

NRR_1 is attached at the 5- or 6-position of the furopyridine ring;

R is hydrogen, C_1-C_4 alkyl, or COR_2;

R_1 is $(CH_2)_nAr$, $CH_2CH{=}CHAr$, or $CH_2C{\equiv}CAr$;

n is 0 to 3;

A is N or NO;

Ar is a 5- or 6-membered aromatic or heteroaromatic ring which contains zero to four nitrogen atoms, zero to one oxygen atoms, and zero to one sulfur atoms;

or: an 8-, 9- or 10-membered fused aromatic or heteroaromatic ring system containing zero to four nitrogen atoms, zero to one oxygen atoms, and zero to one sulfur atoms; any of which may optionally be substituted with one to two substitutents independently selected from: halogen, trifluoromethyl, or C_1-C_4 alkyl;

R_2 is hydrogen, C_1-C_4 alkyl; C_1-C_4 alkoxy; or phenyl ring optionally substituted with one to three of the following substituents: halogen, C_1–C_4 alkyl, C_2–C_4 alkenyl, C_2–C_4 alkynyl, OH, OC_1–C_4 alkyl, CO_2R_5, –CN, $–NO_2$, $–NR_3R_4$, or $–CF_3$;

R_3, R_4 and R_5 are independently hydrogen; C_1-C_4 alkyl; or phenyl ring optionally substituted with one to three of the following substituents: halogen, C_1–C_4 alkyl, C_2–C_4 alkenyl, C_2–C_4 alkynyl, OH, OC_1–C_4 alkyl,–CN; $-NO_2$, or $-CF_3$;
or an enantiomer thereof, and pharmaceutically acceptable salts thereof.

2. A compound according to claim 1, wherein A is N; or an enantiomer thereof, and pharmaceutically acceptable salts thereof.

3. A compound according to claim ~~1 or 2,~~ wherein R_1 is $(CH_2)_nAr$; or an enantiomer thereof, and pharmaceutically acceptable salts thereof.

4. A compound according to claim ~~1 or 2,~~ wherein R_1 is $CH_2CH{=}CHAr$; or an enantiomer thereof, and pharmaceutically acceptable salts thereof.

5. A compound according to claim ~~1 or 2,~~ wherein R_1 is $CH_2C{\equiv}CAr$; or an enantiomer thereof, and pharmaceutically acceptable salts thereof.

6. A compound according to ~~any one of claims 1 to 5,~~ wherein Ar is selected from the group: phenyl ring optionally substituted with one to three of the following substituents: halogen, C_1–C_4 alkyl, C_2–C_4 alkenyl, C_2–C_4 alkynyl, OH, OC_1–C_4 alkyl, CO_2R_5, –CN, $-NO_2$, $-NR_3R_4$, and $-CF_3$; 2-, 3-, or 4-pyridyl; 2-, or 3-furanyl; 2-, or 3-thienyl; 2-, or 4-imidazolyl; 1, 2-, or 3-pyrrolyl; 2-, or 4-oxazolyl; and 3-, or 4-isoxazolyl;
or an enantiomer thereof, and pharmaceutically acceptable salts thereof.

7. A compound according to ~~any one of claims 1 to 5,~~ wherein Ar is selected from ~~the~~ group: 1-, or 2-naphthyl; 2-, 3-, 4-, 5-, 6-, 7-, or 8-quinolyl; 1-, ~~3-~~, 4-, 5-, 6-, ~~7-, or 8-~~ isoquinolyl; 2-, 4-, 5-, 6-, or 7-benzoxazolyl; and 3-, 4-, 5-, 6-, or 7-benzisoxazolyl; or an enantiomer thereof, and pharmaceutically acceptable salts thereof.

8. A compound according to ~~any one of claims 1 to 6,~~ wherein R_3, R_4 and R_5 are independently hydrogen, or C_1-C_4 alkyl;
or an enantiomer thereof, and pharmaceutically acceptable salts thereof.

9. A compound according to ~~any one of claims 1 to 8,~~ wherein n is 1.

10. A compound according to ~~any one of claims 1 to 8~~, wherein R is hydrogen.

11. A compound according to ~~any one of claims 1 to 8,~~ wherein Ar is an heteroaromatic ring.

12. A compound according to ~~any one of claims~~ 1 to 8 wherein n is 1; R is hydrogen and Ar is an heteroaromatic ring.

13. A compound according to claim 1, said compound being:
R-(–)-5'-N-(Phenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];
R-(–)-5'-(2-Pyridylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];
R-(–)-5'-(3-Pyridylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];
R-(–)-5'-(4-Pyridylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];
R-(–)-5'-(2-Furanylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];
R-(–)-5'-(3-Furanylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];
R-(–)-5'-(2-Thienylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];
R-(–)-5'-(2-Imidazolylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(4-Methoxyphenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(4-Chlorophenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(4-Methylphenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(3,4-Dichlorophenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-Acetyl- N-(phenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-Methyl-N-(phenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

(R)-(–)-5'-N-(3-Pyridyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'(3'H)-furo[2,3-b]pyridine];

(R)-(–)-6'-N-(Phenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(3-Thienylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(2-Phenylethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(3-Phenylpropyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(Quinolin-3-ylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(Quinolin-4-ylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(1,4-Benzodioxan-6-ylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(Imidazol-4-ylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(*trans*-3-Phenylprop-2-enyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(Thiazol-2-ylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(3-Methylphenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(2-Chlorophenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(3-Chlorophenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(3-Phenylpropynyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(3-Hydroxyphenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(4-Hydroxyphenylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-[*trans*-3-(4-Pyridinyl)prop-2-enyl]aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-Acetyl-N-(3-thienylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-Methyl-N-(4-pyridylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-Methyl-N-(3-pyridylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-N-(2-Hydroxyethyl)-N-(3-thienylmethyl)aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

or an enantiomer thereof, and pharmaceutically acceptable salts thereof.

14. A compound according to claim 1, said compound being:

R-(–)-5'-(3-Pyridylmethyl) aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];

R-(–)-5'-(4-Pyridylmethyl) aminospiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine];
or an enantiomer thereof, and pharmaceutically acceptable salts thereof.

15. A compound according to ~~any one of claims 1 to 14,~~ for use in therapy.

16. A pharmaceutical composition including a compound as defined in ~~any one of claims~~ 1 to ~~14,~~ in admixture with an inert pharmaceutically acceptable diluent or carrier.

17. The pharmaceutical composition according to claim 16, for use in the treatment or prophylaxis of psychotic disorders or intellectual impairment disorders.

18. The pharmaceutical composition according to claim 16, for use in the treatment or prophylaxis of human diseases or conditions in which activation of the α7 nicotinic receptor is beneficial.

19. The pharmaceutical composition according to claim 16, for use in the treatment or prophylaxis of Alzheimer's disease, learning deficit, cognition deficit, attention deficit, memory loss, Attention Deficit Hyperactivity Disorder, Lewy Body Dementia, anxiety, schizophrenia, mania or manic depression, Parkinson's disease, Huntington's disease, Tourette's syndrome, neurodegenerative disorders in which there is loss of cholinergic synapse, jetlag, cessation of smoking, nicotine addiction including ~~that~~ resulting from exposure to products containing nicotine, pain, or ulcerative colitis.

20. The pharmaceutical composition according to claim 19, for use in the treatment or prophylaxis of Alzheimer's disease, learning deficit, cognition deficit, attention deficit, Lewy Body Dementia, memory loss or Attention Deficit Hyperactivity Disorder.

21. The pharmaceutical composition according to claim 19, for use in the treatment or prophylaxis of anxiety, schizophrenia, mania or manic depression.

22. The pharmaceutical composition according to claim 19, for use in the treatment or prophylaxis of Parkinson's disease, Huntington's disease, Tourette's syndrome, or neurodegenerative disorders in which there is loss of cholinergic synapses.

23. The pharmaceutical composition according to claim 19, for use in the treatment or prophylaxis of jetlag, nicotine addiction including that resulting from exposure to products containing nicotine, pain, or ulcerative colitis.

24. The pharmaceutical composition according to claim 19, for use in the treatment or prophylaxis of Alzheimer's disease.

25. Use of a compound as defined in ~~any one of claims 1 to 14,~~ Claim 1 in the manufacture of a medicament for the treatment or prophylaxis of psychotic disorders or intellectual impairment disorders.

26. The use of a compound as defined in ~~any one of claims 1 to 14,~~ Claim 1 in the manufacture of a medicament for the treatment or prophylaxis of human diseases or conditions in which activation of the α7 nicotinic receptor is beneficial.

27. The use according to claim 25 ~~or claim 26,~~ wherein the condition or disorder is Alzheimer's disease, learning deficit, cognition deficit, attention deficit, memory loss, Attention Deficit Hyperactivity Disorder, Lewy Body Dementia, anxiety, schizophrenia, mania or manic depression, Parkinson's disease, Huntington's disease, Tourette's syndrome, neurodegenerative disorders in which there is loss of cholinergic synapse, jetlag, cessation of smoking, nicotine addiction including that resulting from exposure to products containing nicotine, pain, or ulcerative colitis.

28. The use according to claim 27, wherein the condition or disorder is Alzheimer's disease, learning deficit, cognition deficit, attention deficit, Lewy Body Dementia, memory loss or Attention Deficit Hyperactivity Disorder.

29. The use according to claim 27, wherein the condition or disorder is anxiety, schizophrenia, mania or manic depression.

30. The use according to claim 27, wherein the condition or disorder is Parkinson's disease, Huntington's disease, Tourette's syndrome, or neurodegenerative disorders in which there is loss of cholinergic synapses.

31. The use according to claim 27, wherein the condition or disorder is jetlag, nicotine addiction including that resulting from exposure to products containing nicotine, pain, or ulcerative colitis.

32. The use according to claim 27, wherein the condition or disorder is Alzheimer's disease.

33. A method of treatment or prophylaxis of psychotic disorders or intellectual impairment disorders, which comprises administering a therapeutically effective amount of a compound as defined in ~~any one of claims 1 to 14~~ Claim 1.

34. A method of treatment or prophylaxis of human diseases or conditions in which activation of the α7 nicotinic receptor is beneficial, which comprises administering a therapeutically effective amount of a compound as defined in ~~any one of claims 1 to 14.~~ Claim 1

35. The method according to claim 33 ~~or claim 34,~~ wherein the condition or disorder Alzheimer's disease, learning deficit, cognition deficit, attention deficit, memory loss, Attention Deficit Hyperactivity Disorder, Lewy Body Dementia, anxiety, schizophrenia, mania or manic depression, Parkinson's disease, Huntington's

disease, Tourette's syndrome, neurodegenerative disorders in which there is loss of cholinergic synapse, jetlag, cessation of smoking, nicotine addiction including that resulting from exposure to products containing nicotine, pain, or ulcerative colitis.

36. The method according to claim 33 ~~or claim 34,~~ wherein the condition or disorder is Alzheimer's disease, learning deficit, cognition deficit, attention deficit, Lewy Body Dementia, memory loss or Attention Deficit Hyperactivity Disorder.

37. The method according to claim 33 ~~or claim 34,~~ wherein the condition or disorder is anxiety, schizophrenia, mania or manic depression.

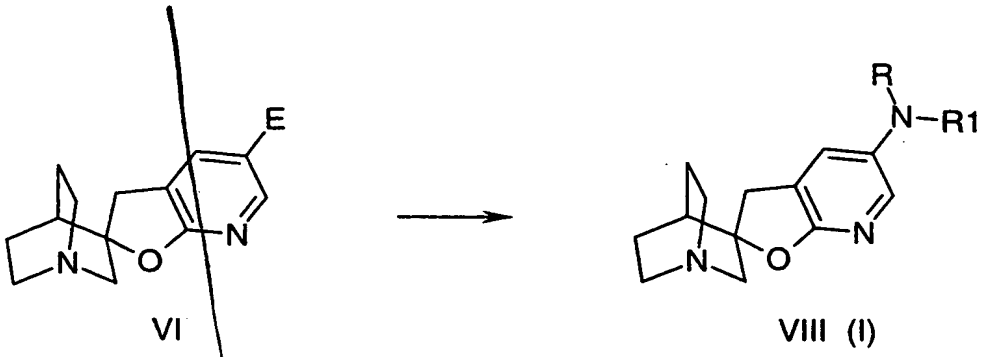
38. The method according to claim 33 ~~or claim 34,~~ wherein the condition or disorder is Parkinson's disease, Huntington's disease, Tourette's syndrome, or neurodegenerative disorders in which there is loss of cholinergic synapses.

39. The method according to claim 33 ~~or claim 34,~~ wherein the condition or disorder is jetlag, nicotine addiction including that resulting from exposure to products containing nicotine, pain, or ulcerative colitis.

40. The method according to claim 33 ~~or claim 34,~~ wherein the condition or disorder is Alzheimer's disease.

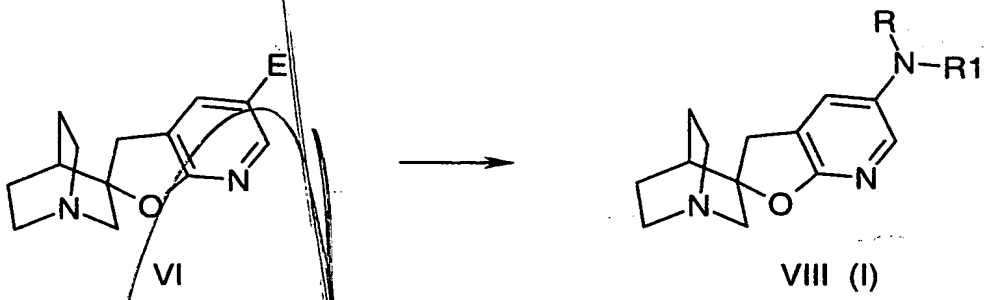
41. A process for preparing a compound of formula I, as defined in ~~any one of claims 1 to 14,~~ claim 1 or an enantiomer thereof, and pharmaceutically acceptable salts thereof, which comprises

a) for preparing compounds wherein NRR1 is positioned in the 5'-position, alkylating or acylating compounds of formula VI, wherein E is halogen, NO_2, or NHR, in a suitable solvent:



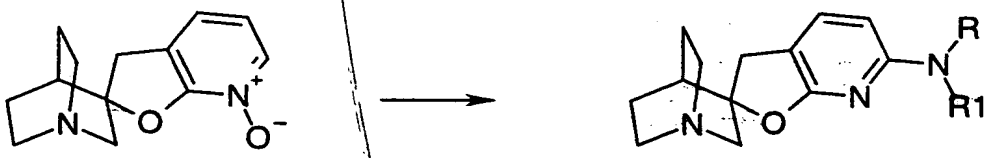
VI VIII (I)

or b) for preparing compounds wherein NRR1 is positioned in the 5'-position, reacting compounds of formula VI, wherein E is halogen, NO_2, or NHR, with an amine in the presence of a suitable organometallic catalyst, base and solvent:



VI VIII (I)

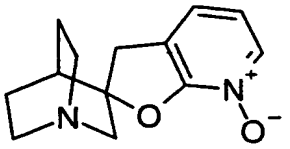
or c) for preparing compounds wherein NRR1 is positioned in the 6'-position, reacting compounds of formula VII, with a halogenating reagent, followed by reaction with an amine in an inert solvent:



VII IX (I)

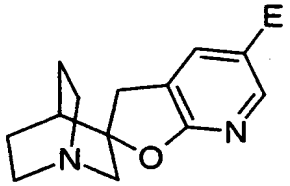
or d) for preparing compounds wherein NRR1 is positioned in the 6'-position, oxidising compounds of formula VIII or IX with a peroxidic reagent in a suitable solvent, followed by partial reduction.

42. A compound of the formula



VII

43. A compound of the formula



VI

where E is NO_2, NHR, or halogen.